

## 2019-nCoV Literature Situation Report (Lit Rep)

May 8, 2020

The scientific literature on COVID-19 is rapidly evolving and these articles were selected for review based on their relevance to Washington State decision making around COVID-19 response efforts. Included in these Lit Reps are some manuscripts that have been made available online as pre-prints but have not yet undergone peer review. Please be aware of this when reviewing articles included in the Lit Reps.

### Key Takeaways

- **An analysis of smartphone location data and healthcare and economic indicators reveals a strong association between greater declines in mobility in counties that are healthier and wealthier, indicating a social distancing privilege gap.**
- **An observational study of 1,446 patients in New York City showed that hydroxychloroquine use was not associated with risk of intubation or death.**
- **A meta-analysis of the diagnostic performance of several serological tests suggests that their pooled diagnostic accuracy is not yet optimal for large-scale prevalence surveys and that their use may currently only be justified in hard-hit regions where prevalence is high.**
- **Researchers from the University of Washington (UW) and Stanford Health Care independently reported a similar frequency of discordant SARS-CoV-2 RT-PCR results (4.3% UW, 2.8% Stanford) among initially negative patients subjected to repeat testing. This suggests that false negative results at the time of initial presentation do occur, but potentially at a lower frequency than what is currently believed.**
- **SARS-CoV-2 can be present in the semen of male patients with COVID-19, including those who were recovering. Future studies are needed to determine if SARS-CoV-2 can be sexually transmitted.**

### Non-Pharmaceutical Interventions

- Using location data from more than 65 million mobile device traces, researchers explored associations between declines in mobility and various healthcare and economic indicators. They observed strong linear gradients in privilege, such that counties in the highest quintile of social distancing mobility restriction had 52% fewer uninsured, 47% more primary care providers, 29% more exercise space, 27% lower food insecurity, 26% less child poverty, and 17% higher incomes compared to least social distancing areas.
- Communities with higher privilege before the pandemic likely have more ability to practice social distancing. Awareness of these systemic constraints should inform the next phase of interventions and allocations of resources to ensure equity.

*Dasgupta et al. (May 8, 2020). Quantifying the Social Distancing Privilege Gap: a Longitudinal Study of Smartphone Movement. Pre-print downloaded May 8 from <https://doi.org/10.1101/2020.05.03.20084624>*

## Transmission

- Kim et al. included 71 participants with laboratory-confirmed SARS-CoV-2 infection who were hospitalized for treatment or isolation and found that 3 were pre-symptomatic and 10 were entirely asymptomatic. Two of the three pre-symptomatic patients had very high levels of virus present during the incubation period (Ct value <20).
- The median time until the first negative RT-PCR (Ct >35) in the entirely asymptomatic carriers was 4.5 (range 2.5-9) days, and all asymptomatic carriers reached the first negative within 14 days after diagnosis. Patients who have COVID-19 may already be infectious before they exhibit symptoms, and 14 days of isolation after diagnosis may be sufficient in entirely asymptomatic cases.

*Kim et al. (May 3, 2020). Viral Kinetics of SARS-CoV-2 in Asymptomatic Carriers and Presymptomatic Patients. International Journal of Infectious Diseases.*

<https://doi.org/10.1016/j.ijid.2020.04.083>

- Li et al. tested semen samples from 38 patients with COVID-19 and detected SARS-CoV-2 from 6 patients (15.8%), including 4 of 15 patients (26.7%) who were at the acute stage of infection and 2 of 23 patients (8.7%) who were recovering. Future studies are needed to determine if SARS-CoV-2 can be sexually transmitted and whether abstinence or condom use should be considered as preventive measures for these patients.

*Li et al. (May 7, 2020). Clinical Characteristics and Results of Semen Tests Among Men With Coronavirus Disease 2019. JAMA Network Open.*

<https://doi.org/10.1001/jamanetworkopen.2020.8292>

## Geographic Spread

- This study used spatial autoregressive models to identify county-level factors associated with COVID-19 mortality in the US. In all counties, population density was significantly associated with higher risk of COVID-19 mortality. In non-urban counties, the proportion of the population who did not speak English, proportion engaged in farm work, and proportion living in poverty was positively associated with COVID-19 mortality. The proportion of uninsured individuals was negatively associated with COVID-19 mortality. Mortality among the uninsured may be being systematically undercounted in county and national level surveillance.

*Fielding-Miller et al. (May 8, 2020). Social Determinants of COVID-19 Mortality at the County Level. Pre-print downloaded May 8 from <https://doi.org/10.1101/2020.05.03.20089698>*

## Testing and Treatment

- A meta-analysis of the diagnostic performance of several serological tests (commercial ELISA or CMIA/CLIA assays and in-house tests) to assess their real-world performance under scenarios of varying proportion of infected individuals found high specificity (pooled estimates of 98% for IgM and 99% for both IgG and total antibodies) but an unsatisfactory pooled sensitivity of 82-85%.
- Even with high specificity, the data suggest that serological tests for large-scale prevalence surveys may only be justifiable in hard-hit areas where the positive predictive value of a positive test would be acceptable, and that they should be used with caution elsewhere.

*Caini et al. (May 8, 2020). Meta-Analysis of Diagnostic Performance of Serological Tests for SARS-CoV-2 Antibodies and Public Health Implications. Pre-print downloaded May 8 from*

<https://doi.org/10.1101/2020.05.03.20084160>

- Geleris et al. conducted an observational study of the association between hydroxychloroquine use and intubation or death among 1,446 consecutive patients at a large medical center in New York City. During a median follow-up of 22.5 days, 59% received hydroxychloroquine either within 24 or 48 hours after presentation to the emergency department, and 25% experienced a primary endpoint (either intubation or death). Those who were treated with hydroxychloroquine were more severely ill at baseline than those were not.
- There was no association between hydroxychloroquine use and intubation or death (HR 1.04, 95% CI 0.82-1.32). While the results do not support either benefit or harm from hydroxychloroquine, the authors recognize the limitations of the observational design and emphasize the need for randomized trial evidence.

*Geleris et al. (May 7, 2020). Observational Study of Hydroxychloroquine in Hospitalized Patients with Covid-19. The New England Journal of Medicine. <https://doi.org/10.1056/NEJMoa2012410>*

- Two independent research teams from the University of Washington (UW) and Stanford Health Care reported a similar frequency of discordant SARS-CoV-2 RT-PCR results among initially negative patients subjected to repeat testing. Among 626 patients who were initially test-negative and re-tested within 7 days, repeat testing yielded a positive result in 3.5% of cases (4.3% UW, 2.8% Stanford). The majority (96.5%) of patients with an initial negative result who warranted re-evaluation remained negative on subsequent tests performed within this window.
- These observations suggest that false negative results at the time of initial presentation do occur, but potentially at a lower frequency than what is currently believed.

*Long et al. (May 8, 2020). Occurrence and Timing of Subsequent SARS-CoV-2 RT-PCR Positivity Among Initially Negative Patients. Pre-print downloaded May 8 from <https://doi.org/10.1101/2020.05.03.20089151>*

- Lowe et al. compared the testing results of SARS-CoV-2 between three commercial assays for SARS-CoV-2 (Xpert Xpress SARS-CoV-2, cobas, and Lightmix Modular SARS) using 37 nasopharyngeal (NP) swabs with lower levels of SARS-CoV-2 RNA (30 with Ct value between 30-33.9, 22 with Ct  $\geq$ 34, and 5 negative for SARS-CoV-2). The overall concordance was 86.5% (32/37), including a 100% concordance for samples with moderate viral concentrations (Ct between 30 to -33.9), but a discordance of 22.7% (5/22) amongst samples with lower viral concentrations (Ct  $\geq$ 34). Testing of SARS-CoV-2 on the three commercial assays was comparable for NP swabs with moderate Ct values, while high Ct values were less concordant.

*Lowe et al. (Apr 28, 2020). Detection of Low Levels of SARS-CoV-2 RNA from Nasopharyngeal Swabs Using Three Commercial Molecular Assays. Journal of Clinical Virology. <https://doi.org/10.1016/j.jcv.2020.104387>*

## Clinical Characteristics and Health Care Setting

- Among patients hospitalized for COVID-19 (n=103), compared to healthy controls (n=13), there were slight lower CD4+T cells counts but a severe lower CD8+T cell counts in COVID-19 patients. COVID-19 patients with severe disease showed significant decreases in T cell subset counts compared to mild-to-moderate patients. This suggests that T cell subset counts, particularly elevated CD4/CD8 ratios could potentially be used as discriminatory biomarkers for diagnosis and severity prediction.

*Jiang et al. (May 7, 2020). T Cell Subset Counts in Peripheral Blood Can Be Used as Discriminatory Biomarkers for Diagnosis and Severity Prediction of COVID-19. Journal of Infectious Diseases. <https://doi.org/10.1093/infdis/jiaa252>*

## Mental Health and Personal Impact

- Bhatia estimates impacts of unemployment in the US during the COVID-19 pandemic on suicide and all-cause mortality by extrapolating from a study of unemployment and suicide rate during the 2007-2010 Great Recession and a meta-analysis of 40 studies evaluating the relationship between unemployment and all-cause mortality. They predict 7,444 excess deaths from suicide in the coming year and 556,000 avoidable deaths from all causes over the next 10 years due to unemployment.
- Decision makers can incorporate indirect health impacts in constructing policies to strike a balance between the benefits and costs of mitigation.

*Bhatia. (May 8, 2020). Quantitative Estimation of Covid-19 Related Unemployment On Suicide and Excess Mortality in the United States. Pre-print downloaded May 8 from <https://doi.org/10.1101/2020.05.02.20089086>*

## Modeling and Prediction

- Basu et al. fit a statistical model to COVID-19 case fatality rates over time in 116 US counties and estimated the symptomatic infection fatality rate among symptomatic cases (IFR-S) to be 1.3% (95% CI 0.6-2.1%). Estimates by county varied from 0.5% to 3.6% (estimated IFR-S for seasonal flu is 0.1%).
- The author acknowledges the conservative nature of the estimate and that the overall IFR would be lower, since cases that recover without symptoms are not accounted for in their model.

*Basu. (May 7, 2020). Estimating The Infection Fatality Rate Among Symptomatic COVID-19 Cases In The United States. Health Affairs (Project Hope). <https://doi.org/10.1377/hlthaff.2020.00455>*

## Public Health and Policy

- The CDC COVID-19 response team reports on factors associated with spread of SARS-CoV-2 in the US. The first confirmed COVID-19 case in the US was reported on January 21, 2020. The outbreak appeared contained through February, and then accelerated rapidly in March. Factors contributing to accelerated spread included continued travel-associated importations, large gatherings, introductions into high-risk workplaces and densely populated areas, and cryptic transmission resulting from limited testing and asymptomatic and pre-symptomatic spread.
- Factors that amplified the March acceleration as well as mitigation strategies that were implemented can inform public health decisions as preparing for potential re-emergences.

*Schuchat. (May 8, 2020). Public Health Response to the Initiation and Spread of Pandemic COVID-19 in the United States, February 24-April 21, 2020. MMWR.*

<https://doi.org/10.15585/mmwr.mm6918e2>

## Other Resources and Commentaries

- [Towards Effective COVID-19 Vaccines: Updates, Perspectives and Challenges \(Review\)](#) - International Journal of Molecular Medicine (May 6)
- [Shared Ventilation in the Era of COVID-19: A Theoretical Consideration of the Dangers and Potential Solutions](#) – Respiratory Care (May 1)
- [Gene of the Month: The 2019-NCoV/SARS-CoV-2 Novel Coronavirus Spike Protein](#) – Journal of Clinical Pathology (May 6)
- [The Pathogenicity of SARS-CoV-2 in HACE2 Transgenic Mice](#) – Nature (May 7)

*Report prepared by the UW MetaCenter for Pandemic Preparedness and Global Health Security and the START Center in collaboration with and on behalf of WA DOH COVID-19 Incidence Management Team*